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10/667,216	09/19/2003	Shaker A. Mousa	2747/1021	7027

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EXAMINER	
LAU, JONATHAN S	
ART UNIT	PAPER NUMBER
1623	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/667,216	MOUSA, SHAKER A.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,6,43,49-54,56-59 and 61-94* is/are pending in the application.

4a) Of the above claim(s) *64-90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,6,43,49-54,56-59,61-63 and 91-94* is/are rejected.

7)☒ Claim(s) *54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 31 Dec 2007, in which independent claim 1 was amended to change to the breadth and scope of the claim and new claims 91-94 are added.

Claims 1, 2, 5, 6, 43, 49-54, 56-59 and 61-94 are pending in the current application. Claims 64-90, drawn to a non-elected invention, are withdrawn. Independent claim 1 has been amended to change to the breadth and scope of the claim and new claims 91-94 have been added.

This application is a domestic application, filed 19 Sep 2003; and claims benefit of provisional application 60/411,851, filed 20 Sep 2002.

However, the parent application provisional application 60/411,851, filed 20 Sep 2002, upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for the instant claims 1, 2, 5, 6, 43, 49-59, 61-63 and 91-94 of this application since the parent application are not seen to disclose the limitation, "wherein the super-sulfated oxidized heparin fraction has a chemical structure of a first oxidized heparin fraction after the first oxidized heparin fraction has been O-sulfated by sulfate substitution at oxygen bonds at vertexes of repeating units of the first oxidized heparin fraction" in the independent claim 1. Written description for O-sulfation at C2 of iduronic acid units and N-sulfation and O-sulfation at C2 of glucosamine units may be found in Figure 1, or for from about 50% to about 100% of primary hydroxyls in glucosamine residues and secondary hydroxyl groups in disaccharide units are substituted by O-sulfate esters in paragraph 29 on page 9, lines 26-28, however no support is found for "O-sulfated by

sulfate substitution at oxygen bonds at vertexes of repeating units", which is a broader scope than the disclosed structure and more specific than the genus disclosed in the specification. Thus, the filing date of the instant claims is deemed to be the filing date of the instant application, 19 Sep 2003. If applicant disagrees, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the earlier priority applications. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

Rejections Withdrawn

Applicant's amendment, filed 31 Dec 2007, with respect to the rejection under 35 U.S.C. 103(a) of claims 1,2, 5, 6, 43, 49-54, 56-59 and 61-63 over Mascellani et al. (Mascellani) (U.S. Patent 4,973,580) in combination with Weitz et al. (Weitz) (U.S. Patent 6,075,013) in view of Cohen et al. (Cohen) (U.S. Patent 5,908,837) in combination with Scholander (U.S. Patent 6,461,665) has been fully considered and is persuasive because the amended claim introduces the new limitation, "wherein the super-sulfated oxidized heparin fraction has a chemical structure of a first oxidized heparin fraction after the first oxidized heparin fraction has been O-sulfated by sulfate substitution at oxygen bonds at vertexes of repeating units of the first oxidized heparin fraction." The rejection of claims 1, 2, 5, 6, 43, 49-54, 56-59 and 61-63 has been WITHDRAWN.

Claim Objections

Claim 54 is objected to because of the following informalities: minor typographical errors, such as "thiotepa", presumably referring to the compound thioTEPA, and "no classic alkylators", which may refer to non-classic alkylators or any agent that is not a classic alkylator. Appropriate correction is required.

The following new grounds of rejection are necessitated by Applicant's amendment, filed 31 Dec 2007, in which independent claim 1 was amended to change to the breadth and scope of the claim and new claims 91-94 were added.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Amended claim 1 recites, "wherein the super-sulfated oxidized heparin fraction comprises a sulfate to carboxylate ratio sufficiently high to **fully inhibit** angiogenesis," emphasis added

Nature of the invention: An oxidized heparin fraction having a molecular weight of from about 2,000 to about 4,000 daltons, wherein the oxidized heparin fraction is

super-sulfated such that the oxidized heparin fraction comprises an anticoagulant reduction characteristic and an angiogenesis inhibition characteristic, capable of fully inhibiting angiogenesis.

The state of the prior art: Inhibit in a biological context is defined as "To decrease, limit, or block the action or function of (an enzyme or organ, for example)." See provided definition of inhibit (definition of inhibit, Dictionary.com, cited in PTO-892). The ordinary definition of inhibit includes completely blocking the action or function of angiogenesis. There is no prior art disclosing completely blocking the action or function of angiogenesis.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: The lack of any prior art disclosing completely blocking the action or function of angiogenesis means that one skilled in the art cannot predict the usefulness of a product capable of completely blocking the action or function of angiogenesis. Therefore the claimed invention is unpredictable.

The Breadth of the claims: The scope of the claims specifically includes a compound that is capable of fully inhibiting angiogenesis.

The amount of direction or guidance presented: The specification speaks generally about the efficiency of the anti-angiogenicity of the compound. See instant specification, paragraph 27 spanning pages 8 and 9.

The presence or absence of working examples: The only working examples provided are reducing the FGF2- stimulated cell tube formation to the level of the Phosphate Buffered Saline (PBS) control. For example, see instant specification, Table

3 on page 29. The observation of a baseline level of the action or function of angiogenesis indicates that the action or function is not completely blocked, or fully inhibited.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as completely blocking the action or function of angiogenesis. See MPEP 2164.

The quantity of experimentation necessary: In order to practice the invention with capabilities beyond those known in the art, (such as reducing the FGF2- stimulated cell tube formation to the level of the Phosphate Buffered Saline (PBS) control) one skilled in the art would undertake a novel and extensive research program to show that the compound was capable of completely blocking the action or function of angiogenesis. Because this research would have to be exhaustive, and because it would involve such a wide and unpredictable scope of compounds, it would constitute an undue and unpredictable experimental burden.

> *Genentech*, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims, Applicants fail to provide information sufficient to practice the claimed invention capable of fully inhibiting angiogenesis.

Amended claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Amended claim 1 recites the limitation, "wherein the super-sulfated oxidized heparin fraction has a chemical structure of a first oxidized heparin fraction after the first oxidized heparin fraction has been O-sulfated by sulfate substitution at oxygen bonds at vertexes of repeating units of the first oxidized heparin fraction." The ordinary definition of vertex is a corner of a polygon; as anhydroglucose is usually drawn as a hexagon, this is interpreted to mean O-sulfation at the oxygen at each corner, or carbon, of the anhydroglucose unit. However, no support for this specific limitation can be found in the application as filed or in the parent provisional application 60/411,851 upon which priority is claimed. Written description for O-sulfation at C2 of iduronic acid units and N-sulfation and O-sulfation at C2 of glucosamine units may be found in Figure 1, or for from about 50% to about 100% of primary hydroxyls in glucosamine residues and secondary hydroxyl groups in disaccharide units are substituted by O-sulfate esters in paragraph 29 on page 9, lines 26-28, however no support is found for "O-sulfated by sulfate substitution at oxygen bonds at vertexes of repeating units", which is a broader scope than the disclosed structure in Figure 1 and more specific than the genus disclosed in the specification in paragraph 29 on page 9, lines 26-28.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Amended claims 2, 5 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Amended claims 2, 5 and 6 currently depend from claim 91.

Amended claim 2 recites the limitation "the first anticoagulant reduction characteristic" in line 2. Amended claim 5 recites the limitation "the second anticoagulant reduction characteristic" in line 2. Amended claim 6 recites the limitation "the first anticoagulant reduction characteristic and the second anticoagulant reduction characteristic" in lines 2-3. There is insufficient antecedent basis for this limitation in the amended claims. New claim 91 depends from amended claim 1. Amended claim 1 recites “an anticoagulant reduction characteristic and an angiogenesis inhibition characteristic,” not a first or second anticoagulant reduction characteristic.

For the purpose of advancing prosecution, Examiner is interpreting amended claims 2, 5 and 6 as being drawn to the first and second anticoagulant reduction characteristic recited in new claim 93.

Claim Rejections - 35 USC § 102

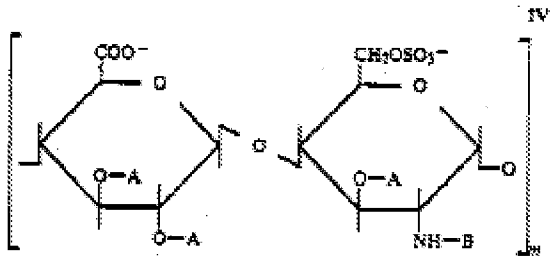
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Amended claims 1, 2, 5, 6, 43, 91-94 are rejected under 35 U.S.C. 102(b) as being anticipated by Naggi et al. (US Patent 4,727,063, issued 23 Feb 1988, cited in PTO-892).

Naggi et al. discloses a depolymerized and supersulfated heparin having a molecular weight between 2000 and 9000 and a sulfation degree of at least 2.5 and the process for its preparation comprising sulfating heparin (abstract). Naggi et al. discloses the heparin treated with sulfuric acid and chlorosulfonic acid, a strong oxidizing agent, to depolymerize and super-sulfate heparin (spanning column 4 lines 66-68 and column 5 lines 1-10), meeting the instant limitations of instant claim 94 and addressing the term "oxidized heparin fraction." The instant specification recites, "The percentage of hydroxyl residues that are oxidized in accordance with the present invention is determined by the length of incubation with the oxidizing agent and/or the quantity of oxidizing agent used," on page 8, lines 24-26, and further recites non-limiting embodiments. The term "oxidized heparin fraction" does not require the hydroxyl residues of the oxidized heparin fraction to be present in the oxidized state, and the term "oxidized heparin fraction" encompasses heparin compounds wherein the hydroxyl residues are not oxidized as indicated by the limitation of instant claim 91, "wherein the sulfate to carboxylate ratio is about 5:1," as a sulfate to carboxylate ratio of 5:1 is possible only when the hydroxyl residues are present in the oxidation state of hydroxyl residues.

Naggi et al. discloses the structure as formula IV,



, wherein m is an integer from 4 to 15, A is H or SO_3^-, and B is SO_3^-or $COCH_3$ (column 6, lines 1-19) . One of ordinary skill in the art would instantly envision the compound where m is 4 and A and B are SO_3^-, a compound with molecular weight of (352+417)*4, or 3,076 daltons, wherein the ratio of sulfate to carboxylates is 5:1, and the hydroxyl groups are 100% substituted as O-sulfate esters, meeting the limitations of instant claims 1 and 91-93. Naggi et al. recites “It is also generally recognized that at the same degree of polymerization, the biological activity of polysaccharides increases with their sulfation degree,” (column 3, lines 42-44), which provides guidance to one of ordinary skill in the art to instantly envision said compound. Naggi et al. discloses the compound in the form of a pharmaceutical composition (column 10, lines 55-57), meeting the limitations of instant claim 43. Naggi et al. discloses the reduction of the anticoagulation reduction characteristic with regards to the activated partial thromboplastin time (APTT) (column 9, lines 7-11 and 47-60), explicitly meeting the limitations of instant claims 5 and 93. Naggi et al. is silent as to an angiogenesis inhibition characteristic and the anticoagulant reduction characteristic in terms of a “percent inhibition of platelet clot strength," but does recite that the depolymerized and supersulfated heparin shows a weak anticoagulant activity (column

5, lines 41-45). Therefore there is reason to believe that the characteristics recited in instant claims 2 and 6 are inherent in the compound disclosed by Naggi et al.

It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Amended claims 1, 43, 49, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naggi et al. (US Patent 4,727,063, issued 23 Feb 1988, cited in PTO-892) in view of Weitz et al. (US Patent 6,075,013, issued 13 Jun 2000, of record).

Naggi et al. discloses as above.

Naggi et al. does not disclose the specific composition further comprising a non-heparin anticoagulant.

Weitz et al. teaches the use of modified low molecular weight heparin (column 10, lines 25-30) obtained by oxidation (column 10, lines 47-53) used in conjunction with

conventional thrombolytic treatments, such as tissue plasminogen activator, an anti-tissue factor compound (column 11, lines 20-30).

It would have been obvious to one of ordinary skill at the time of the invention to combine depolymerized and supersulfated heparin disclosed by Naggi et al. in conjunction with conventional thrombolytic treatments, such as tissue plasminogen activator, an anti-tissue factor compound, as taught by Weitz et al. Both inventions are drawn to antithrombotic compositions. See MPEP 2144.06, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art."

Amended claims 1 and 56-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naggi et al. (US Patent 4,727,063, issued 23 Feb 1988, cited in PTO-892) in view of Conrad et al. (US Patent 5,280,016, issued 18 Jan 1994, cited in PTO-892).

Naggi et al. discloses as above.

Naggi et al. does not specifically disclose a polymeric structure comprising an oxidized heparin fraction, wherein said oxidized heparin fraction is covalently attached to the polymeric structure by surface grafting or copolymerization, non-covalently incorporated into a matrix of the polymeric structure, or encapsulated as a biomedical

material within the polymeric structure, or wherein said biocompatible polymer is ethylene vinyl acetate.

Conrad et al. teaches size separated fractions of depolymerized low molecular weight heparin produced by periodate oxidation (column 3, lines 25-29) that are non-anticoagulant and show antiproliferative activity with respect to smooth muscle cells (abstract), or an angiogenesis inhibition characteristic. Conrad et al. teaches the size separated fractions are treated chemical to produce O-oversulfation to increase activity (column 4, lines 27-37). Conrad et al. teaches the heparin administered in the form of an implant containing biodegradable polymer materials such as collagen, formulated as patches or beads, which is encapsulation as a biomedical material, or by local administration through a continuous release device such as a supporting matrix, which is understood to be non-covalent incorporation into the matrix (column 10, lines 47-50 and 60-63). Conrad et al. teaches the use of the specific polymer ethylene vinyl acetate as the supporting matrix (column 14, lines 34-38).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the depolymerized and supersulfated heparin disclosed by Naggi et al. with the O-oversulfated low molecular weight heparin incorporated into a polymeric structure as taught by Conrad et al. Conrad et al. teaches the size separated fractions are treated chemical to produce O-oversulfation to increase activity (column 4, lines 27-37). Naggi et al. recites “It is also generally recognized that at the same degree of polymerization, the biological activity of polysaccharides increases with their sulfation degree,” (column 3, lines 42-44). Therefore it would have been obvious to one of

ordinary skill in the art at the time of the invention to use of a known technique of supersulfation to improve similar depolymerized low molecular weight heparin in the same way by combining the depolymerized and supersulfated heparin disclosed by Naggi et al. with the O-oversulfated low molecular weight heparin incorporated into a polymeric structure as taught by Conrad et al.

Amended claims 1, 43 and 51-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naggi et al. (US Patent 4,727,063, issued 23 Feb 1988, cited in PTO-892) in view of Conrad et al. (US Patent 5,280,016, issued 18 Jan 1994, cited in PTO-892) as applied to claims 1 and 56-59 above, and further in view of Kerbel et al. (Cancer and Metastasis Reviews, 2001, 20, p79-86, cited in PTO-892).

Naggi et al. in view of Conrad et al. discloses as above. Conrad et al. makes explicit that the antiproliferative activity with respect to smooth muscle cells, or angiogenesis inhibition characteristic, inherent in the compound disclosed by Naggi et al. was recognized in the prior art.

Naggi et al. in view of Conrad et al. does not disclose the specific composition further comprising a non-heparin angiogenic inhibitor, or a cytotoxic or chemotherapeutic agent.

Kerbel et al. teaches the use of combinations of angiogenesis inhibitors (page 82, right column, lines 9-11), such as chemotherapy drugs such as microtubule agents and anti-angiogenic drugs (page 82, right column, lines 14-17). Kerbel et al. teaches the use of combinations of specific drugs such as DC101 antibody to VEGF (vascular

endothelial growth factor) receptor-2 (page 83, spanning left column line 23 and right column lines 1-2); thalidomide, interferon alpha, and low molecular weight heparin (page 83, right column, lines 18-22) and angiostatin, endostatin, and interleukin-12 (page 84, left column, lines 1-3).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the depolymerized and supersulfated heparin taught by Naggi et al. in view of Conrad et al. with the combinations of angiogenesis inhibitors taught by Kerbel et al. See MPEP 2144.06, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." Kerbel et al. teaches the use of low molecular weight heparin in said combinations. One of ordinary skill in the art would be motivated to combine the specific depolymerized and supersulfated heparin taught by Naggi et al. in view of Conrad et al. with the combinations of angiogenesis inhibitors taught by Kerbel et al. because Naggi et al. recites “It is also generally recognized that at the same degree of polymerization, the biological activity of polysaccharides increases with their sulfation degree,” (column 3, lines 42-44).

Amended claims 1, 56, 61 and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naggi et al. (US Patent 4,727,063, issued 23 Feb 1988, cited in PTO-892) in view of Scholander (US Patent 6,461,665, issued 08 Oct 2002, of record).

Naggi et al. discloses as above.

Naggi et al. does not disclose the polymeric structure wherein said oxidized heparin fraction is covalently attached to the polymeric structure by surface grafting or by copolymerization.

Scholander teaches a surface modified to have improved antithrombogenic activity by attaching heparin to the surface to be modified (abstract), comprising reacting heparin with the surface (column 4, lines 25-40), or surface grafting, or by reacting the heparin with a polymer layer and reacting the heparin-containing polymer with other polymers (column 5, lines 1-30), such as when the heparin is reacted with the later from step (a). The reaction of a heparin-containing polymer with other polymers can be interpreted as copolymerization.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the depolymerized and supersulfated heparin disclosed by Naggi et al. with the surface modified to have improved antithrombogenic activity by attaching heparin to the surface to be modified taught by Scholander. One of ordinary skill in the art would be motivated to combine the specific depolymerized and supersulfated heparin disclosed by Naggi et al. with the surface modified to have improved antithrombogenic activity taught by Scholander because Naggi et al. recites “It is also generally recognized that at the same degree of polymerization, the biological activity of polysaccharides increases with their sulfation degree,” (column 3, lines 42-44).

Conclusion

No claim is found to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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